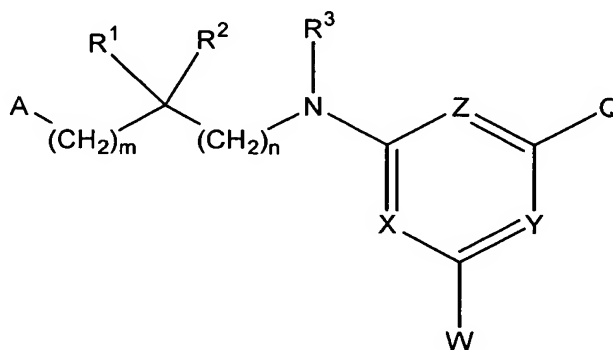


## CLAIMS

1. A compound of formula

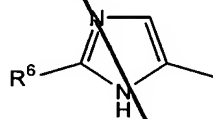
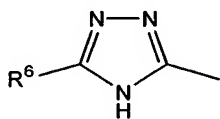


wherein:

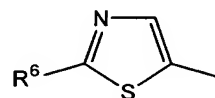
- (a) all of X, Y and Z are CH; or (b) one of X, Y and Z is N and the rest of X, Y and Z are CH; or (c) two of X, Y and Z are N and the other of X, Y and Z is CH; or (d) all of X, Y and Z are N;

A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-

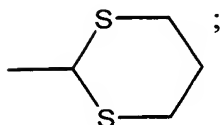


or



10 A<sup>2</sup> is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-;

Q is chosen from heteroaryl, aryl, -CH<sub>2</sub>R<sup>13</sup>, -CH=N-OCH<sub>3</sub>, and



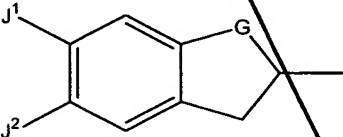
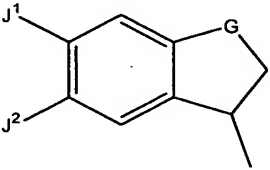
W is chosen from H, Cl, F, R<sup>8</sup>, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, -OR<sup>8</sup>, -SR<sup>8</sup>, -NR<sup>9</sup>R<sup>10</sup> and -NHC(O)R<sup>11</sup>, with the proviso that when two of X, Y and Z are

15 N and Q is imidazolyl, W may not be H, Cl, F or R<sup>8</sup>;

R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl, C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-

a'  
Cont

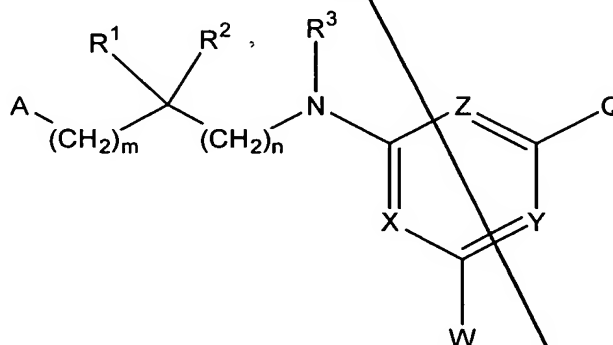
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- alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;
- 20 R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;
- R<sup>3</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;
- 25 R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to three aryl or heteroaryl residues,
- 
and

, wherein J<sup>1</sup>
- and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;
- 30 R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;
- 35 R<sup>6</sup> is aryl;
- R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;
- R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;
- 40 R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl,

Q1  
cont

- 45 R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or  
 R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;  
 R<sup>11</sup> is aryl;  
 50 R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxyacetyl, methoxyacetyl and aryl;  
 R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;  
 m is zero or one; and  
 n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

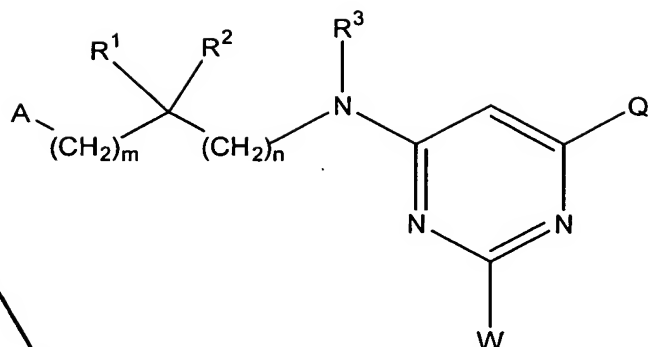
2. A pyrimidine according to claim 1 of formula



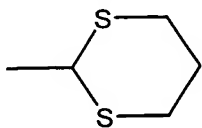
wherein:

two of X, Y and Z are N and the third is CH.

3. A 4-pyrimidinamine according to claim 2, wherein Z is CH, having the formula

a'  
cont

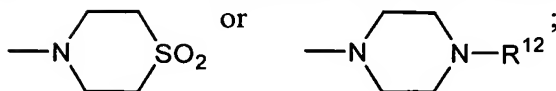
4. A 4-pyrimidinamine according to claim 3 wherein Q is chosen from imidazolyl, methylimidazolyl, pyrrolyl, methylpyrrolyl, pyrazolyl, methylpyrazolyl, hydroxymethylimidazolyl, (dimethylaminomethyl)imidazolyl, furanyl, methylfuranyl, thienyl, oxazolyl, thiazolyl, pyridinyl, quinolinyl, 1-methylpyrimidin-2-onyl, phenyl, fluorophenyl, hydroxymethyl, tetrahydropyranyloxymethyl, imidazolylmethyl, pyrrolylmethyl, -CH=N-OCH<sub>3</sub>, and



5. A 4-pyrimidinamine according to claim 4 wherein:  
Q is chosen from pyrrol-1-yl, imidazol-1-yl, furan-3-yl, 2-methylimidazol-1-yl and 4-methylimidazol-1-yl;

A is R<sup>4</sup>R<sup>5</sup>N-C(O)-;

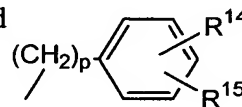
W is Cl, NHR<sup>9</sup>, N(CH<sub>3</sub>)R<sup>9</sup>, OR<sup>8</sup>, SR<sup>8</sup>, R<sup>8</sup>, morpholin-4-yl,



- R<sup>1</sup> is chosen from alkyl, cycloalkyl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl ;  
R<sup>2</sup>, R<sup>3</sup> and R<sup>5</sup> are H;  
R<sup>8</sup> is C<sub>1</sub>-C<sub>4</sub>-alkylaryl

20  $R^9$  is chosen from hydrogen, alkyl, substituted alkyl,  $(C_1-C_4)$ -alkoxy,  $C_1-C_4$ -alkylcycloalkyl,  $C_1-C_4$ -alkylaryl, heterocyclyl,  $C_1-C_4$ -alkylheteroaryl,  $C_1-C_4$ -alkylheterocyclyl; and  
m and n are zero.

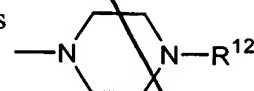
6. A 4-pyrimidinamine according to claim 5 wherein W is  $NHR^9$  and  
 $R^9$  is chosen from hydrogen; methyl; ethyl; 2,2,2-trifluoroethyl; allyl; cyclopropyl; 2-cyanoethyl; propargyl; methoxy; methoxyethyl; cyclopropyl; cyclopropylmethyl; (methylthio)ethyl; 3-methoxypropyl; 3-pyridyl; 2-(3-pyridyl)ethyl; 2-(2-pyridyl)ethyl; 3-pyridylmethyl; 4-pyridylmethyl; 4-pyridylmethyl-N-oxide; 2-pyridazinylmethyl; sulfolan-3-yl; 3-tetrahydrofuranyl; 2-tetrahydrofuranylmethyl; 3-(1-imidazolyl)propyl; 1-*t*-butoxycarbonyl-4-piperidiny; 1-*t*-butoxycarbonyl-4-piperidinylmethyl; 2-(hydroxyimino)propyl; 2-(methoxyimino)propyl; 2-oxo-1-propyl; and



wherein

$R^{14}$  is chosen from H, Cl, F, CN,  $NO_2$ ,  $SO_2NH_2$ ,  $CF_3$ ,  $COOCH_3$ ,  $OCH_3$ , OH,  $SO_2CH_3$ ,  $N(CH_3)_2$  and COOH;  
 15  $R^{15}$  is chosen from H,  $OCH_3$  and Cl; and  
 p is 1 or 2.

7. A 4-pyrimidinamine according to claim 5 wherein W is



and

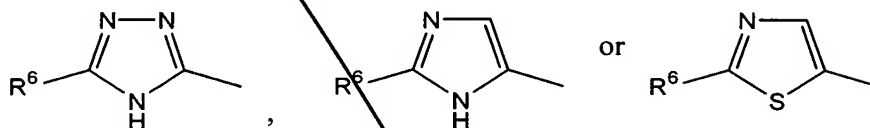
*A<sup>1</sup> Cont*

R<sup>12</sup> is t-butoxycarbonyl, methoxyacetyl or phenyl.

8. A 4-pyrimidinamine according to claim 2 ✓ wherein

Z is CH;

A is



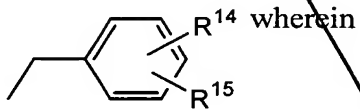
5 R<sup>1</sup> is chosen from n-butyl; cyclohexylmethyl; cyclopentylmethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-t-butoxycarbonyl-4-piperidinyl; 4-chlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

10 R<sup>2</sup> and R<sup>3</sup> are H;

Q is imidazolyl or pyrrolyl;

W is NHR<sup>9</sup>; and

R<sup>9</sup> is alkyl, cycloalkyl or



15 R<sup>14</sup> is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

R<sup>15</sup> is chosen from H, OCH<sub>3</sub> and Cl.

9. A pyrimidine according to claim 2 ✓ wherein:

A is R<sup>4</sup>R<sup>5</sup>N-C(O)-

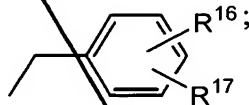
5 R<sup>1</sup> is chosen from isopropyl; n-butyl; cyclohexylmethyl; cyclopentylmethyl; naphthylmethyl; cyclohexylethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl;

benzyl; 2-thienylmethyl; 1-*t*-butoxycarbonyl-4-piperidinyl; 4-methoxybenzyl; 4-chlorobenzyl; 3,4-dichlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl; and

10  $R^2$ ,  $R^3$  and  $R^5$  are H.

10. A pyrimidine according to claim 9 wherein:

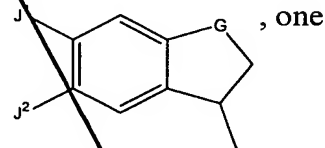
$R^4$  is pyridinyl, pyridinylmethyl, tetrahydronaphthalenyl, indanylmethyl, furanylmethyl, substituted phenyl, or



15  $R^{16}$  is chosen from H, Cl, F, CN,  $\text{NO}_2$ ,  $\text{SO}_2\text{NH}_2$ ,  $\text{CF}_3$ ,  $\text{CH}_3$ ,  $\text{COOCH}_3$ ,  $\text{OCH}_3$ ,  $\text{SO}_2\text{CH}_3$ ,  $\text{SOCH}_3$ ,  $\text{N}(\text{CH}_3)_2$ , tetrazol-5-yl,  $\text{CONH}_2$ ,  $\text{C}(=\text{NOH})\text{NH}_2$  and  $\text{COOH}$ ; and

$R^{17}$  is chosen from H,  $\text{OCH}_3$ , F and Cl.

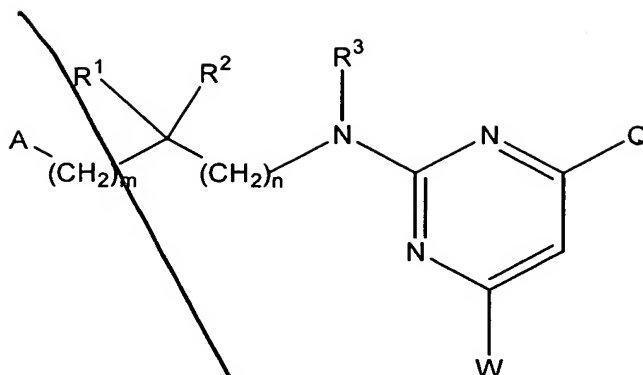
11. A pyrimidine according to claim 9 wherein  $R^4$  is



20 of  $J^1$  and  $J^2$  is H and the other is H, Cl or CN and G is chosen from  $-\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2-$ ,  $-\text{OCH}_2-$ ,  $-\text{O}-$  and  $-\text{CH}_2\text{N}(\text{lower alkyl})-$ .

12. A 2-pyrimidinamine according to claim 2, wherein Y is CH, having the formula

Q'  
cont



13. A 2-pyrimidinamine according to claim 11 wherein Q is chosen from imidazolyl, pyrrolyl, pyridinyl, fluorophenyl and 2-thienyl.

14. A 2-pyrimidinamine according to claim 13 wherein

A is  $R^4R^5N-C(O)-$ ;

5 W is H, Cl,  $NHR^9$  or  $OR^8$ ;

$R^1$  is chosen from alkyl and  $C_1-C_3$ -alkylcycloalkyl;

$R^2$ ,  $R^3$  and  $R^5$  are H;

$R^4$  is  $C_1-C_4$ -alkylaryl or  $C_1-C_4$ -alkylheteroaryl;

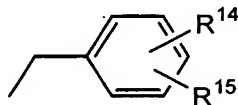
$R^8$  is  $C_1-C_4$ -alkylaryl;

10  $R^9$  is chosen from hydrogen, alkyl, fluoroalkyl,  $(C_1-C_4$ -alkoxy)alkyl,  $(C_1-C_4$ -alkylthio)alkyl,  $C_1-C_4$ -alkylcycloalkyl,  $C_1-C_4$ -alkylaryl, heterocyclyl,  $C_1-C_4$ -alkylheteroaryl,  $C_1-C_4$ -alkylheterocyclyl; and

m and n are zero.

15. A 2-pyrimidinamine according to claim 14 wherein W is  $NHR^9$  and

$R^9$  is

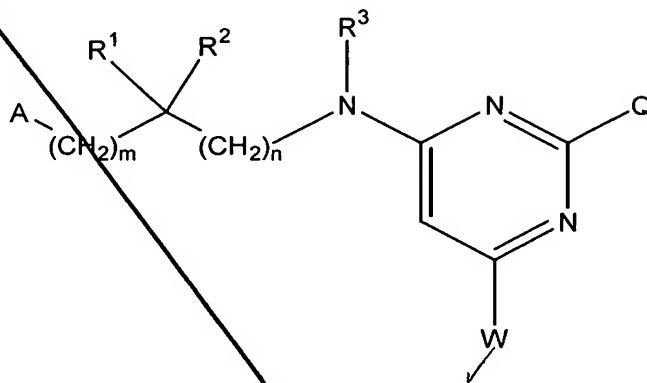


$R^{14}$  is chosen from H, F, Cl, CN,  $NO_2$ ,  $SO_2NH_2$ ,  $CF_3$ ,  $COOCH_3$ ,  $OCH_3$ ,  $SO_2CH_3$ ,  $N(CH_3)_2$  and  $COOH$ ; and



5  $R^{15}$  is chosen from H,  $OCH_3$  and Cl.

16. A 4-pyrimidinamine according to claim 2, wherein X is CH, having the formula



17. A 4-pyrimidinamine according to claim 16 wherein Q is chosen from imidazolyl and pyrrolyl and m and n are zero.

18. A 4-pyrimidinamine according to claim 17 wherein:

A is  $R^4R^5N-C(O)-$ ;

W is  $NHR^9$ ;

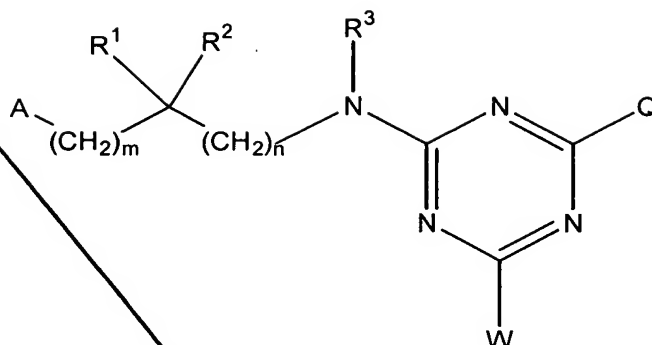
$R^1$  is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

$R^2$ ,  $R^3$  and  $R^5$  are H; and

$R^4$  and  $R^9$  are benzyl or substituted benzyl.

19. A triazine according to claim 1, wherein all of X, Y, and Z are N, having the formula

Qe'  
Cont



20. A triazine according to claim 19 wherein Q is chosen from imidazolyl and pyrrolyl.

21. A triazine according to claim 20 wherein:

A is  $R^4R^5N-C(O)-$ ;

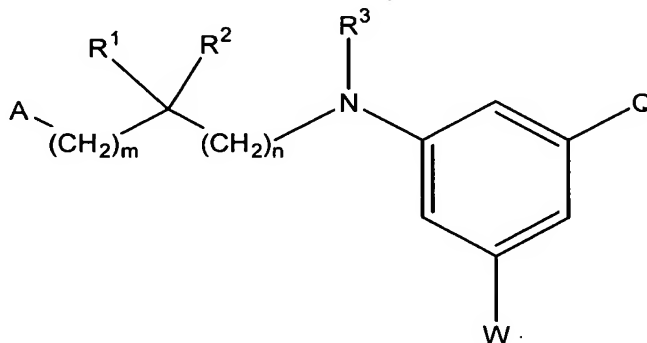
W is  $NHR^9$ ;

R<sup>1</sup> is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

R<sup>2</sup>, R<sup>3</sup> and R<sup>5</sup> are H; and

R<sup>4</sup> and R<sup>9</sup> are benzyl or substituted benzyl.

22. An aniline according to claim 1, wherein all of X, Y and Z are CH, having the formula



wherein Q is chosen from imidazolyl and pyrrolyl.

23. An aniline according to claim 22 wherein:

A is  $R^4R^5N-C(O)-$ ;

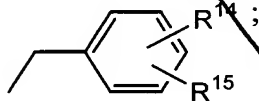
W is  $NHR^9$ ;

$R^1$  is chosen from alkyl, cycloalkyl,  $C_1-C_3$ -alkylaryl and  $C_1-C_3$ -alkylcycloalkyl;

$R^2$ ,  $R^3$  and  $R^5$  are H;

$R^4$  is  $C_1-C_4$ -alkylaryl;

$R^9$  is



$R^{14}$  is chosen from H, Cl, CN,  $NO_2$ ,  $SO_2NH_2$ ,  $CF_3$ ,  $COOCH_3$ ,  $OCH_3$ ,  $SO_2CH_3$ ,  $N(CH_3)_2$  and  $COOH$ ;

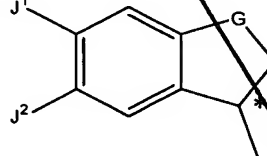
$R^{15}$  is chosen from H,  $OCH_3$  and Cl; and

m and n are zero.

24. A compound according to claim 1 wherein m and n are zero and  $R^2$  is H having the R configuration at the carbon to which  $R^2$  is attached.

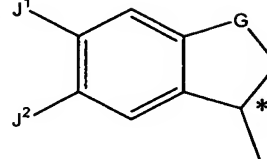
25. A compound according to claim 1 wherein m and n are zero and  $R^1 = R^2$ .

26. A compound according to claim 1 wherein  $R^4$  is  $J^1$



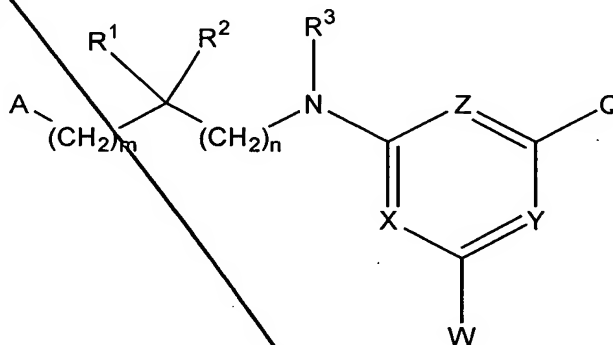
having the R configuration at the carbon indicated with an asterisk.

27. A pyrimidine according to claim 12 wherein R<sup>4</sup> is J<sup>1</sup>



having the R configuration at the carbon indicated with an asterisk.

28. A compound of formula

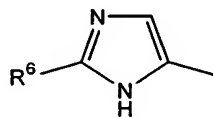
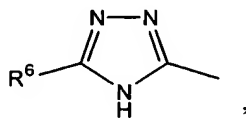


wherein:

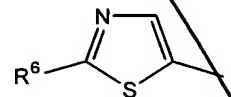
- (a) all of X, Y and Z are CH; or (b) one of X, Y and Z is N and the rest of X, Y and Z are CH; or (c) two of X, Y and Z are N and the other of X, Y and Z is CH; or (d) all of X, Y and Z are N;

A is A<sup>1</sup> or A<sup>2</sup>;

A<sup>1</sup> is R<sup>4</sup>R<sup>5</sup>N-C(O)-



or

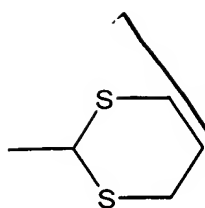


A<sup>2</sup> is chosen from R<sup>7</sup>C(O)NH-, R<sup>7</sup>S(O)<sub>2</sub>NH-, R<sup>4</sup>NH-, and R<sup>4</sup>O-;

Q is chosen from aryl, -CH<sub>2</sub>R<sup>13</sup>, -CH=N-OCH<sub>3</sub>, and

a'  
cont

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heteroaryl other than 1-imidazolyl and 1-triazolyl;

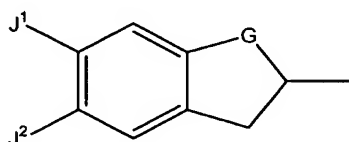
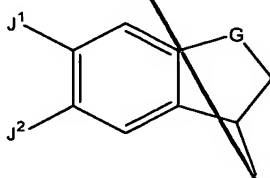
W is chosen from H, Cl, F, R<sup>8</sup>, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, -OR<sup>8</sup>, -SR<sup>8</sup>, -NR<sup>9</sup>R<sup>10</sup> and -NHC(O)R<sup>11</sup>, with the proviso that when two of X, Y and Z are N and Q is imidazolyl, W may not be H, Cl, F or R<sup>8</sup>;

R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl, C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;

R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;

R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;

R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to three aryl or heteroaryl residues,

and  , wherein J<sup>1</sup>

and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;

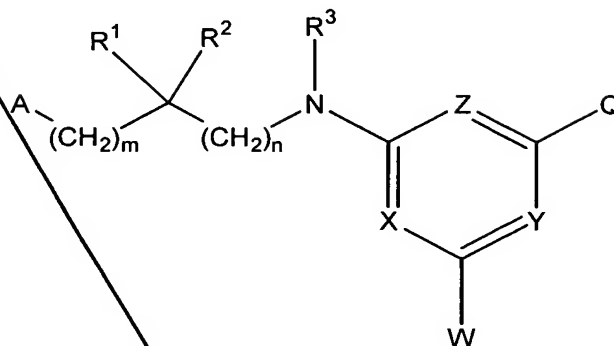
*A<sup>1</sup>*  
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- ~~R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;~~
- ~~R<sup>6</sup> is aryl;~~
- ~~R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;~~
- ~~R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;~~
- ~~R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;~~
- ~~R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or~~
- ~~R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;~~
- ~~R<sup>11</sup> is aryl;~~
- ~~R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;~~
- ~~R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;~~
- ~~m is zero or one; and~~
- ~~n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.~~

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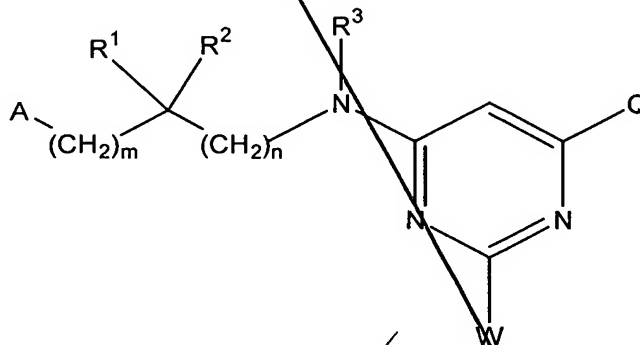
29. A pyrimidine according to claim 28 of formula



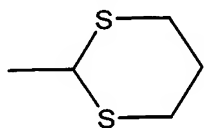
wherein:

two of X, Y and Z are N and the third is CH.

30. A 4-pyrimidinamine according to claim 29, wherein Z is CH, having the formula



31. A 4-pyrimidinamine according to claim 30 wherein Q is chosen from methylimidazolyl, pyrrolyl, methylpyrrolyl, pyrazolyl, methylpyrazolyl, furanyl, methylfuranyl, thienyl, oxazolyl, thiazolyl, pyridinyl, quinolinyl, 1-methylpyrimidin-2-onyl, phenyl, fluorophenyl, hydroxymethyl, 2-imidazolyl, tetrahydropyranyloxymethyl, imidazolylmethyl, pyrrolylmethyl,  $-\text{CH}=\text{N}-\text{OCH}_3$  and

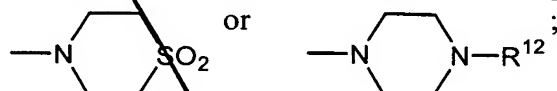


32. A 4-pyrimidinamine according to claim 31 wherein:

Q is chosen from pyrrol-1-yl, imidazol-1-yl, furan-3-yl, 2-methylimidazol-1-yl and 4-methylimidazol-1-yl;

A is  $R^4 R^5 N C(O)-$ ;

W is Cl,  $NHR^7$ ,  $N(CH_3)R^9$ ,  $OR^8$ ,  $SR^8$ ,  $R^8$ , morpholin-4-yl,



$R^1$  is chosen from alkyl, cycloalkyl,  $C_1$ - $C_3$ -alkylaryl,  $C_1$ - $C_3$ -alkylcycloalkyl,  $C_1$ - $C_3$ -alkylheterocyclyl,  $C_1$ - $C_3$ -alkylheteroaryl;

15  $R^2$ ,  $R^3$  and  $R^5$  are H;

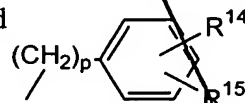
$R^8$  is  $C_1$ - $C_4$ -alkylaryl

$R^9$  is chosen from hydrogen, alkyl, substituted alkyl,  $(C_1-C_4)$ -alkoxy,  $C_1$ - $C_4$ -alkylcycloalkyl,  $C_1$ - $C_4$ -alkylaryl, heterocyclyl,  $C_1$ - $C_4$ -alkylheteroaryl,  $C_1$ - $C_4$ -alkylheterocyclyl; and

20 m and n are zero.

33. A 4-pyrimidinamine according to claim 32 wherein W is  $NHR^9$  and

$R^9$  is chosen from hydrogen; methyl; ethyl; 2,2,2-trifluoroethyl; allyl; cyclopropyl; 2-cyanoethyl; propargyl; methoxy; methoxyethyl; cyclopropyl; cyclopropylmethyl; (methylthio)ethyl; 3-methoxypropyl; 3-pyridyl; 2-(3-pyridyl)ethyl; 2-(2-pyridyl)ethyl; 3-pyridylmethyl; 4-pyridylmethyl; 4-pyridylmethyl-N-oxide; 2-pyridazinylmethyl; sulfolan-3-yl; 3-tetrahydrofuranyl; 2-tetrahydrofuranylmethyl; 3-(1-imidazolyl)propyl; 1-*t*-butoxycarbonyl-4-piperidinyll; 1-*t*-butoxycarbonyl-4-piperidinylmethyl; 2-(hydroxyimino)propyl; 2-(methoxyimino)propyl; 2-oxo-1-propyl; and

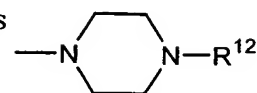




A'  
cont

- wherein
- 15  $R^{14}$  is chosen from H, Cl, F, CN,  $\text{NO}_2$ ,  $\text{SO}_2\text{NH}_2$ ,  $\text{CF}_3$ ,  $\text{COOCH}_3$ ,  $\text{OCH}_3$ , OH,  $\text{SO}_2\text{CH}_3$ ,  $\text{N}(\text{CH}_3)_2$  and  $\text{COOH}$ ;
- $R^{15}$  is chosen from H,  $\text{OCH}_3$  and Cl; and
- p is 1 or 2.

34. A 4-pyrimidinamine according to claim 32 wherein W is



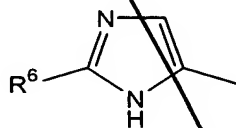
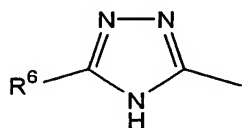
and

$R^{12}$  is t-butoxycarbonyl, methoxyacetyl or phenyl.

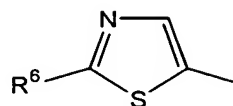
35. A 4-pyrimidinamine according to claim 29 wherein

Z is CH;

A is



or



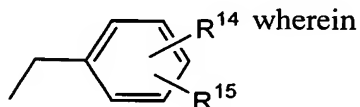
- 5  $R^1$  is chosen from n-butyl; cyclohexylmethyl; cyclopentylmethyl; 2-methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl; benzyl; 2-thienylmethyl; 1-t-butoxycarbonyl-4-piperidinyl; 4-chlorobenzyl; 2-pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

10  $R^2$  and  $R^3$  are H;

Q is pyrrolyl;

W is  $\text{NHR}^9$ ; and

$R^9$  is alkyl, cycloalkyl or



Q1  
cont

R<sup>14</sup> is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, COOCH<sub>3</sub>, OCH<sub>3</sub>,  
SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

R<sup>15</sup> is chosen from H, OCH<sub>3</sub> and Cl.

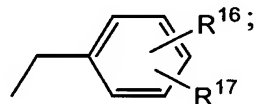
36. A pyrimidine according to claim 29 wherein:

A is R<sup>4</sup>R<sup>5</sup>N-C(O)-

R<sup>1</sup> is chosen from isopropyl; n-butyl; cyclohexylmethyl;  
cyclopentylmethyl; naphthylmethyl; cyclohexylethyl; 2-  
methylpropyl; 3-methyl-1-butyl; cyclohexyl; 2,2-dimethylpropyl;  
benzyl; 2-thienylmethyl; 1-*t*-butoxycarbonyl-4-piperidinyl; 4-  
methoxybenzyl; 4-chlorobenzyl; 3,4-dichlorobenzyl; 2-  
pyranylmethyl; 4-pyranylmethyl; 4-pyranyl and 1,1-dimethylethyl;

R<sup>2</sup>, R<sup>3</sup> and R<sup>5</sup> are H;

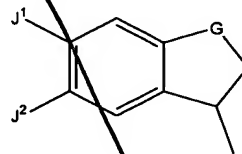
10 R<sup>4</sup> is pyridinyl, pyridinylmethyl, indanylmethyl, furanylmethyl,  
tetrahydronaphthalenyl, substituted phenyl, or



R<sup>16</sup> is chosen from H, Cl, F, CN, NO<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CF<sub>3</sub>, CH<sub>3</sub>, COOCH<sub>3</sub>,  
OCH<sub>3</sub>, SO<sub>2</sub>CH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> and COOH; and

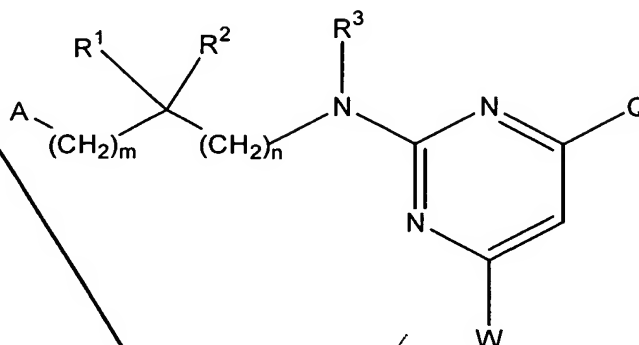
R<sup>17</sup> is chosen from H, OCH<sub>3</sub>, F and Cl.

37. A pyrimidine according to claim 29 wherein R<sup>4</sup> is



38. A pyrimidine according to claim 37 wherein one of J<sup>1</sup> and J<sup>2</sup> is H and the  
other is H, Cl or CN and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -O- and  
-CH<sub>2</sub>N(lower alkyl)-.

39. A 2-pyrimidinamine according to claim 29, wherein Y is CH, having the formula



40. A 2-pyrimidinamine according to claim 39 wherein Q is chosen from pyrrolyl, pyridinyl, fluorophenyl and 2-thienyl.

41. A 2-pyrimidinamine according to claim 40 wherein

A is  $R^4R^5N-C(O)-$ ;

5 W is H, Cl,  $NHR^9$  or  $OR^8$ ;

$R^1$  is chosen from alkyl and  $C_1-C_3$ -alkylcycloalkyl;

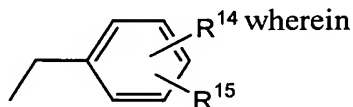
$R^2$ ,  $R^3$  and  $R^5$  are H;

$R^4$  is  $C_1-C_4$ -alkylaryl or  $C_1-C_4$ -alkylheteroaryl;

$R^8$  is  $C_1-C_4$ -alkylaryl;

10  $R^9$  is chosen from hydrogen, alkyl, fluoroalkyl,  $(C_1-C_4$ -alkoxy)alkyl,  $(C_1-C_4$ -alkylthio)alkyl,  $C_1-C_4$ -alkylcycloalkyl,  $C_1-C_4$ -alkylaryl, heterocyclyl,  $C_1-C_4$ -alkylheteroaryl,  $C_1-C_4$ -alkylheterocyclyl; and m and n are zero.

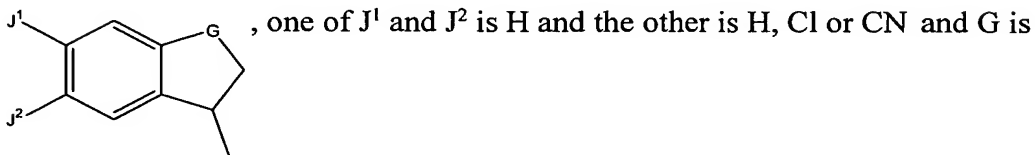
42. A 2-pyrimidinamine according to claim 41 wherein W is  $NHR^9$  and  $R^9$  is



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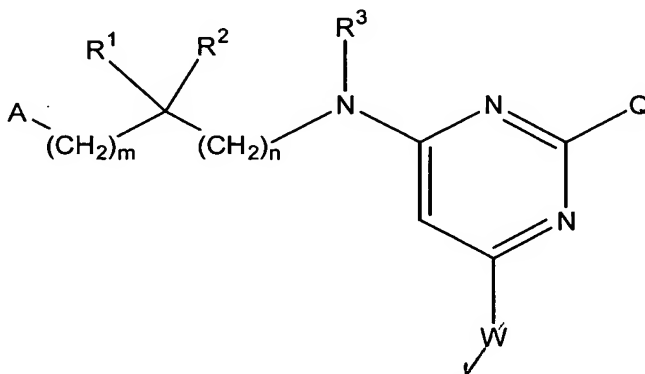
- 5  $R^{14}$  is chosen from H, F, Cl, CN,  $NO_2$ ,  $SO_2NH_2$ ,  $CF_3$ ,  $COOCH_3$ ,  $OCH_3$ ,  $SO_2CH_3$ ,  $N(CH_3)_2$  and  $COOH$ ; and
- $R^{15}$  is chosen from H,  $OCH_3$  and Cl.

43. A 2-pyrimidineamine according to claim 39 wherein  $R^4$  is



chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-OCH_2-$ ,  $-O-$  and  $-CH_2N(\text{lower alkyl})-$ .

44. A 4-pyrimidinamine according to claim 29, wherein X is CH, having the formula



45. A 4-pyrimidinamine according to claim 44 wherein Q is pyrrolyl and m and n are zero.

46. A 4-pyrimidinamine according to claim 45 wherein:

A is  $R^4R^5N-C(O)-$ ;

W is  $NHR^9$ ;

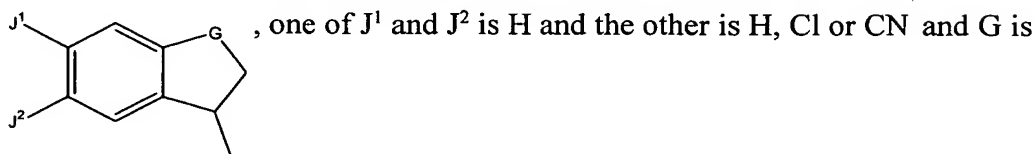
$R^1$  is chosen from cyclohexylmethyl; 2-methylpropyl and 3-methyl-1-butyl;

5

*a' cont*  
 $R^2$ ,  $R^3$  and  $R^5$  are H; and

$R^4$  and  $R^9$  are benzyl or substituted benzyl.

47. A 4-pyrimidineamine according to claim 44 wherein  $R^4$  is



10 chosen from  $-CH_2-$ ,  $-CH_2CH_2-$ ,  $-OCH_2-$ ,  $-O-$  and  $-CH_2N(\text{lower alkyl})-$ .

48. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 1.

49. A pharmaceutical composition according to claim 48 additionally comprising a steroidal or nonsteroidal antiinflammatory drug (NSAID).

50. A pharmaceutical composition according to claim 48 additionally comprising a nonsteroidal antiinflammatory drug (NSAID).

51. A pharmaceutical composition according to claim 50 wherein said NSAID is chosen from arylpropionic acids, arylacetic acids, arylbutyric acids, fenamic acids, arylcarboxylic acids, pyrazoles, pyrazolones, salicylic acids; and oxicams.

52. A pharmaceutical composition according to claim 48 additionally comprising a cyclooxygenase inhibitor.

53. A pharmaceutical composition according to claim 52 wherein said cyclooxygenase inhibitor is ibuprofen or a salicylic acid derivative.

A'  
Cont

54. A pharmaceutical composition according to claim 48 additionally comprising a selective cyclooxygenase-2 inhibitor. ✓

55. A pharmaceutical composition according to claim 54 wherein said selective cyclooxygenase-2 inhibitor is rofecoxib or celecoxib. ✓

56. A pharmaceutical composition according to claim 48 additionally comprising a selective cyclooxygenase-1 inhibitor. ✓

57. A pharmaceutical composition according to claim 48 additionally comprising a steroidal antiinflammatory drug. ✓

58. A pharmaceutical composition according to claim 57 wherein said steroidal antiinflammatory drug is chosen from finasteride, beclomethasone and hydrocortisone. ✓

59. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 28. ✓

60. A pharmaceutical composition according to claim 59 additionally comprising a steroidal or nonsteroidal antiinflammatory drug (NSAID). ✓

61. A pharmaceutical composition according to claim 59 additionally comprising a nonsteroidal antiinflammatory drug (NSAID). ✓

62. A pharmaceutical composition according to claim 61 wherein said NSAID is chosen from arylpropionic acids, arylacetic acids, arylbutyric acids, fenamic acids, arylcarboxylic acids, pyrazoles, pyrazolones, salicylic acids; and oxicams. ✓

63. A pharmaceutical composition according to claim 59 additionally comprising a cyclooxygenase inhibitor. ✓

64. A pharmaceutical composition according to claim 63 wherein said cyclooxygenase inhibitor is ibuprofen or a salicylic acid derivative. ✓

65. A pharmaceutical composition according to claim 59 additionally comprising a selective cyclooxygenase-2 inhibitor. ✓

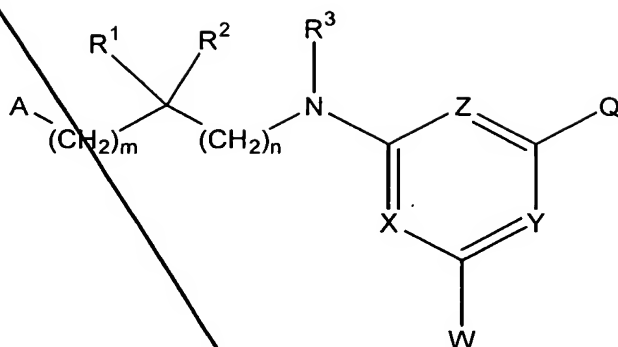
66. A pharmaceutical composition according to claim 65 wherein said selective cyclooxygenase-2 inhibitor is rofecoxib or celecoxib. ✓

67. A pharmaceutical composition according to claim 59 additionally comprising a selective cyclooxygenase-1 inhibitor. ✓

68. A pharmaceutical composition according to claim 59 additionally comprising a steroidal antiinflammatory drug. ✓

69. A pharmaceutical composition according to claim 68 wherein said steroidal antiinflammatory drug is chosen from finasteride, beclomethasone and hydrocortisone. ✓

70. A method of treating a condition resulting from inappropriate bradykinin receptor activity comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of formula I

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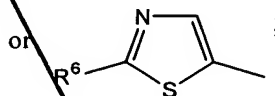
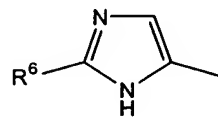
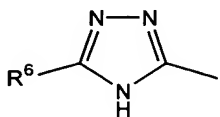
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wherein:

(a) all of X, Y and Z are CH; or (b) one of X, Y and Z is N and the rest of X, Y and Z are CH; or (c) two of X, Y and Z are N and the other of X, Y and Z is CH; or (d) all of X, Y and Z are N;

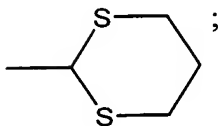
A is  $A^1$  or  $A^2$ ;

$A^1$  is  $R^4R^5N-C(O)-$



$A^2$  is chosen from  $R^7C(O)NH-$ ,  $R^7S(O)_2NH-$ ,  $R^4NH-$ , and  $R^4O-$ ;

Q is chosen from heteroaryl, aryl,  $-CH_2R^{13}$ ,  $-CH=N-OCH_3$ , and



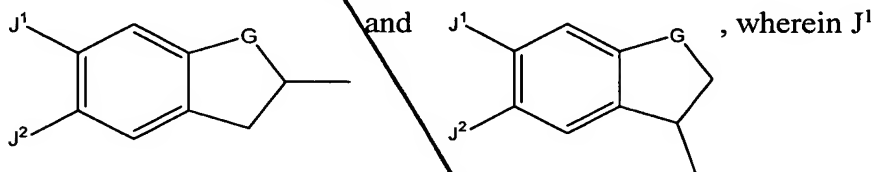
W is chosen from H, Cl, F,  $R^8$ ,  $C_1-C_4$ -alkylaryl,  $-OR^8$ ,  $-SR^8$ ,  $-NR^9R^{10}$  and  $-NHC(O)R^{11}$ , with the proviso that when two of X, Y and Z are N and Q is imidazolyl, W may not be H, Cl, F or  $R^8$ ;



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- R<sup>1</sup> is chosen from alkyl, cycloalkyl, alkenyl, C<sub>1</sub>-C<sub>3</sub>-alkylcycloalkyl, heterocyclyl, C<sub>1</sub>-C<sub>3</sub>-alkylheterocyclyl, aryl, C<sub>1</sub>-C<sub>3</sub>-alkylaryl, heteroaryl, C<sub>1</sub>-C<sub>3</sub>-alkylheteroaryl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkyloxy)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)alkyl, (C<sub>1</sub>-C<sub>3</sub>-alkylthio)cycloalkyl and (C<sub>1</sub>-C<sub>3</sub>-alkylsulfonyl)alkyl;
- R<sup>2</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together form a 5- to 7-membered ring structure optionally containing O, S or NR<sup>12</sup>;
- R<sup>3</sup> is H or C<sub>1</sub>-C<sub>6</sub>-alkyl, or, when n is zero, R<sup>2</sup> and R<sup>3</sup> taken together may form a 6-membered ring, which may be fused to a six-membered saturated or aromatic carbocycle;
- R<sup>4</sup> is chosen from H, aryl, heteroaryl, C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with from one to three aryl or heteroaryl residues,



- and J<sup>2</sup> are independently chosen from H, F, Cl, CN, NO<sub>2</sub> and CH<sub>3</sub>, and G is chosen from -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -OCH<sub>2</sub>-, -CH<sub>2</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>O-, -OCH<sub>2</sub>CH<sub>2</sub>-, -O-, -N(lower alkyl)-, -N(lower alkyl)CH<sub>2</sub>-, -CH<sub>2</sub>N(lower alkyl)-, -S-, -SO-, -SO<sub>2</sub>-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>SO-, -SOCH<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, and -SO<sub>2</sub>CH<sub>2</sub>-;
- R<sup>5</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, with the proviso that both R<sup>3</sup> and R<sup>5</sup> cannot be alkyl;
- R<sup>6</sup> is aryl;
- R<sup>7</sup> is aryl or C<sub>1</sub>-C<sub>3</sub>-alkylaryl;
- R<sup>8</sup> is chosen from alkyl, aryl, heteroaryl, substituted alkyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

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cont*

R<sup>9</sup> is chosen from H, alkyl, alkenyl, substituted alkyl, cycloalkyl, aryl, alkoxy, heteroaryl, fluoroalkyl, C<sub>1</sub>-C<sub>4</sub>-alkylcycloalkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxy)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkoxycarbonyl)alkyl, (C<sub>1</sub>-C<sub>4</sub>-alkylthio)alkyl, heterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylheterocyclyl, C<sub>1</sub>-C<sub>4</sub>-alkylaryl, and C<sub>1</sub>-C<sub>4</sub>-alkylheteroaryl;

R<sup>10</sup> is H or C<sub>1</sub>-C<sub>3</sub>-alkyl, or

R<sup>9</sup> and R<sup>10</sup> taken together may form a 5- to 7-membered ring structure optionally containing O, S, SO, SO<sub>2</sub> or NR<sup>12</sup>, said ring optionally substituted with -OH, -CN, -COOH or -COOCH<sub>3</sub>;

R<sup>11</sup> is aryl;

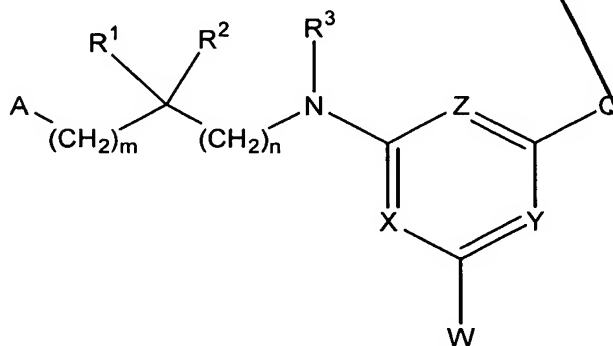
R<sup>12</sup> is chosen from H, C<sub>1</sub>-C<sub>3</sub>-alkyl, alkoxycarbonyl, methoxyacetyl and aryl;

R<sup>13</sup> is chosen from -OH, -OTHP, 1-imidazolyl, and 1-pyrrolyl;

m is zero or one; and

n is zero or one, with the proviso that when A is A<sup>2</sup>, m and n cannot both be zero.

71. A method according to claim 70 wherein said compound is a pyrimidine of the formula



wherein:

two of X, Y and Z are N and the third is CH.

*a' cont*

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72. The method according to claim 70 wherein said condition resulting from inappropriate bradykinin receptor activity is diabetic vasculopathy, post-capillary resistance or diabetic symptoms associated with insulinitis.

73. The method according to claim 72 wherein said diabetic symptoms associated with insulinitis comprise hyperglycemia, diuresis, proteinuria and increased nitrite and kallikrein urinary excretion.

74. The method according to claim 70 wherein said condition resulting from inappropriate bradykinin receptor activity is inflammation, edema, liver disease, asthma, rhinitis, or septic shock.

75. The method according to claim 70 wherein said condition resulting from inappropriate bradykinin receptor activity is pain or hyperalgesia.

76. The method according to claim 75 wherein said pain is chronic pain, pain associated with inflammation or dental pain.

77. The method of treating pain or hyperalgesia according to claim 75 additionally comprising administering a steroidal or nonsteroidal antiinflammatory drug (NSAID).

78. The method of treating pain or hyperalgesia according to claim 77 wherein an NSAID is administered.

79. The method of treating pain or hyperalgesia according to claim 75 additionally comprising administering a cyclooxygenase inhibitor.

Q1  
cont

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80. The method of treating pain or hyperalgesia according to claim 79 wherein said cyclooxygenase inhibitor is a selective cyclooxygenase-2 inhibitor. ✓

81. The method of treating pain or hyperalgesia according to claim 79 wherein said cyclooxygenase inhibitor is a selective cyclooxygenase-1 inhibitor. ✓

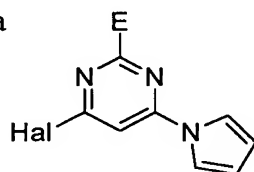
82. The method according to claim 70 wherein said condition resulting from inappropriate bradykinin receptor activity is multiple sclerosis. ✓

83. The method according to claim 70 wherein said condition resulting from inappropriate bradykinin receptor activity is atherosclerosis. ✓

84. The method according to claim 70 wherein said condition resulting from inappropriate bradykinin receptor activity is Alzheimer's disease or closed head trauma. ✓

85. A method for stimulating hair growth or preventing hair loss comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound formula I according to claim 70. ✓

86. A compound of formula



wherein E is halogen or methylthio and Hal is halogen.

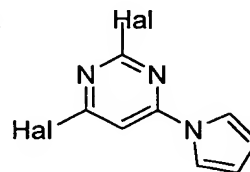
87. A compound according to claim 86 wherein Hal is chlorine. ✓

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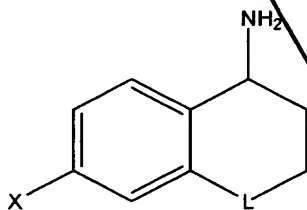
88. A compound according to claim 86 wherein Hal is fluorine.

89. A compound according to claim 86 wherein E is methylthio and Hal is chlorine.

90. A compound according to claim 86 of formula

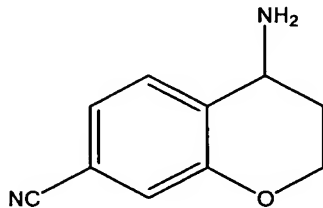


91. A compound of formula

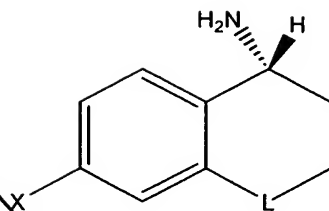


wherein  $\text{X}$  is  $-\text{CN}$  or halogen and  $\text{L}$  is  $-\text{CH}_2-$  or  $-\text{N}(\text{CH}_3)-$ .

92. A compound of formula

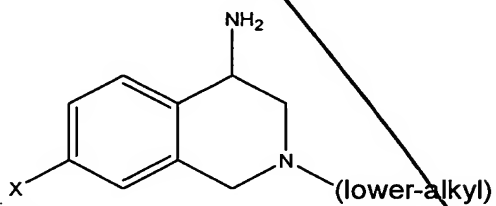


93. A compound of formula

a'  
cont

having the R absolute stereochemistry at the asymmetric carbon, wherein X is -CN or halogen and L is -CH<sub>2</sub>-, -O- or -N(CH<sub>3</sub>)-.

94. A compound of formula



wherein X is -CN or halogen.